

**A1**

This patent application includes a computer program listing appendix (Appendix), which contains the source code for the software used in carrying out the examples in accordance with the present invention. The Appendix is contained on one compact disc submitted in duplicate and designated as Copy 1 and Copy 2. The Appendix is in a single file that is 292 kB in size and designated "computer program listing appendix U.S. Serial No. 09-021,721". The file was created on 02/02/1998 and is a Microsoft Word document. The material in the Appendix is incorporated herein by reference.

Please replace the paragraphs beginning on page 46, line 4, to page 50, line 35 with the following paragraphs (for the convenience of the Examiner, Applicant is also including a clean copy of pages 46-50, which may be substituted for the existing pages):

GTCCAAAAAGGGTCAGTCTACCTCCGCCATAAAAAACTCATGTTCAAGA (target complement sequence) (SEQ ID NO: 9)

	T <sub>m</sub> (°C)	ΔG <sub>MFOLD</sub>	
GTCCAAAAAGGGTCAGTCTACCTCC	71.77	-1.20	SEQ ID NO: 10
TCCAAAAAGGGTCAGTCTACCTCCC	71.99	-1.20	SEQ ID NO: 11
CCAAAAAGGGTCAGTCTACCTCCCG	70.78	-1.20	SEQ ID NO: 12
AAAAAAAGGGTCAGTCTACCTCCCCC	71.23	-1.20	SEQ ID NO: 13
AAAAAAGGGTCAGTCTACCTCCCGCC	73.07	-1.20	SEQ ID NO: 14
AAAAGGGTCAGTCTACCTCCGCCA	75.68	-1.20	SEQ ID NO: 15
AAAGGGTCAGTCTACCTCCGCCAT	77.53	-1.20	SEQ ID NO: 16
AAAGGGTCAGTCTACCTCCGCCATA	79.03	-1.20	SEQ ID NO: 17
AGGGTCAGTCTACCTCCGCCATAA	79.03	-1.20	SEQ ID NO: 18
GGGTCAGTCTACCTCCGCCATAAA	76.85	-1.20	SEQ ID NO: 19
GGTCAGTCTACCTCCGCCATAAAA	73.10	-0.80	SEQ ID NO: 20
GTCAGTCTACCTCCGCCATAAAAAA	69.50	0.90	SEQ ID NO: 21
TCAGTCTACCTCCGCCATAAAAAAA	65.60	0.90	SEQ ID NO: 22
CAGTCTACCTCCGCCATAAAAAAAC	64.96	0.90	SEQ ID NO: 23
AGTCTACCTCCGCCATAAAAAAACT	65.48	1.10	SEQ ID NO: 24
GTCAGTCTACCTCCGCCATAAAAAACTC	66.36	2.40	SEQ ID NO: 25
TCTACCTCCGCCATAAAAAACTCA	64.97	2.90	SEQ ID NO: 26
CTACCTCCGCCATAAAAAACTCAT	63.96	2.70	SEQ ID NO: 27
TACCTCCGCCATAAAAAACTCATG	62.58	1.10	SEQ ID NO: 28
ACCTCCGCCATAAAAAACTCATGT	65.10	0.40	SEQ ID NO: 29
CCTCCGCCATAAAAAACTCATGTT	64.96	0.10	SEQ ID NO: 30
CTCCCGCCATAAAAAACTCATGTT	63.37	-0.10	SEQ ID NO: 31
TCCCGCCATAAAAAACTCATGTTCA	62.86	-0.10	SEQ ID NO: 32
CCCGCCATAAAAAACTCATGTTCAA	60.47	-0.10	SEQ ID NO: 33
CCGCCATAAAAAACTCATGTTCAAG	57.98	-0.10	SEQ ID NO: 34
CGCCATAAAAAACTCATGTTCAAGA	56.20	-0.10	SEQ ID NO: 35

**A2**

Next, the oligonucleotide sequences are filtered on the basis of T<sub>m</sub>. A high and low cut-off value may be selected, for example, 60°C ≤ T<sub>m</sub> ≤ 85°C. Thus, oligonucleotides having T<sub>m</sub> values falling within the above range are retained. Those outside the range are

discarded, which is indicated below by lining out of those oligonucleotides and parameter values.

GTCCAAAAAGGGTCAGTCTACCTCCCGCCATAAAAAACTCATGTTCAAGA (target complement sequence) (SEQ ID NO: 9)

	$T_m$ (°C)	$\Delta G_{MFOLD}$	
GTCCAAAAAGGGTCAGTCTACCTCC	71.77	-1.20	SEQ ID NO: 10
TCCAAAAAGGGTCAGTCTACCTCCC	71.99	-1.20	SEQ ID NO: 11
CACAAAGGGTCAGTCTACCTCCG	70.78	-1.20	SEQ ID NO: 12
CAAAAGGGTCAGTCTACCTCCGC	71.23	-1.20	SEQ ID NO: 13
AAAAGGGTCAGTCTACCTCCGCC	73.07	-1.20	SEQ ID NO: 14
AAAAGGGTCAGTCTACCTCCGCCA	75.68	-1.20	SEQ ID NO: 15
AAAGGGTCAGTCTACCTCCGCCAT	77.53	-1.20	SEQ ID NO: 16
AAGGGTCAGTCTACCTCCGCCATA	79.03	-1.20	SEQ ID NO: 17
ACGGTCAGTCTACCTCCGCCATAA	79.03	-1.20	SEQ ID NO: 18
GGGTCACTTACCTCCGCCATAAA	76.85	-1.20	SEQ ID NO: 19
GGTCAGTCTACCTCCGCCATAAAA	73.10	-0.80	SEQ ID NO: 20
GTCAGTCTACCTCCGCCATAAAAAA	69.50	0.90	SEQ ID NO: 21
TCAGTCTACCTCCGCCATAAAAAA	65.60	0.90	SEQ ID NO: 22
CACTCTACCTCCGCCATAAAAAAC	64.96	0.90	SEQ ID NO: 23
ACTCTACCTCCGCCATAAAAAACT	65.48	1.10	SEQ ID NO: 24
GTCTACCTCCGCCATAAAAAACTC	66.36	2.40	SEQ ID NO: 25
TCTACCTCCGCCATAAAAAACTCA	64.97	2.90	SEQ ID NO: 26
CTACCTCCGCCATAAAAAACTCAT	63.96	2.70	SEQ ID NO: 27
TACCTCCGCCATAAAAAACTCATG	62.58	1.10	SEQ ID NO: 28
ACCTCCCGCCATAAAAAACTCATGT	65.10	0.40	SEQ ID NO: 29
CCTCCCGCCATAAAAAACTCATGTT	64.96	0.10	SEQ ID NO: 30
CTCCCGCCATAAAAAACTCATGTT	63.37	-0.10	SEQ ID NO: 31
TCCCGCCATAAAAAACTCATGTTCA	62.86	-0.10	SEQ ID NO: 32
CCCGCCATAAAAAACTCATGTTCAA	60.47	-0.10	SEQ ID NO: 33
CCGCCATAAAAAACTCATGTTCAAG	57.98	-0.10	SEQ ID NO: 34
CCGCCATAAAAAACTCATGTTCAAGA	56.20	-0.10	SEQ ID NO: 35

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cont

Next, the oligonucleotide sequences remaining after the above exercise are filtered on the basis of  $\Delta G_{MFOLD}$  and are retained if the value is greater than - 0.4. Those oligonucleotides with a  $\Delta G_{MFOLD}$  less than - 0.4 are discarded, which is indicated below by double lining out of those oligonucleotides and parameter values.

GTCCAAAAAGGGTCAGTCTACCTCCGCCATAAAAAACTCATGTTCAAGA (target complement sequence) (SEQ ID NO: 9)

	$T_m$ (°C)	$\Delta G_{MFOLD}$	
GTCCAAAAAGGGTCAGTCTACCTCCGCCATAAAAAACTCATGTTCAAGA	71.77	-1.20	SEQ ID NO: 10
	71.99	-1.20	SEQ ID NO: 11
	70.78	-1.20	SEQ ID NO: 12
	71.23	-1.20	SEQ ID NO: 13
	73.07	-1.20	SEQ ID NO: 14
	75.68	-1.20	SEQ ID NO: 15
	77.53	-1.20	SEQ ID NO: 16
	79.03	-1.20	SEQ ID NO: 17
	79.03	-1.20	SEQ ID NO: 18
	76.85	-1.20	SEQ ID NO: 19
	73.10	-0.80	SEQ ID NO: 20
GTCAGTCTACCTCCGCCATAAAAAA	69.50	0.90	SEQ ID NO: 21
TCAGTCTACCTCCGCCATAAAAAAA	65.60	0.90	SEQ ID NO: 22
CAGTCTACCTCCGCCATAAAAAAAC	64.96	0.90	SEQ ID NO: 23
AGTCTACCTCCGCCATAAAAAAACT	65.48	1.10	SEQ ID NO: 24
GTCTACCTCCGCCATAAAAAAACTC	66.36	2.40	SEQ ID NO: 25
TCTACCTCCGCCATAAAAAAACTCA	64.97	2.90	SEQ ID NO: 26
CTACCTCCGCCATAAAAAAACTCAT	63.96	2.70	SEQ ID NO: 27
TACCTCCGCCATAAAAAAACTCATG	62.58	1.10	SEQ ID NO: 28
ACCTCCCGCCATAAAAAAACTCATGT	65.10	0.40	SEQ ID NO: 29
CCTCCCGCCATAAAAAAACTCATGTT	64.96	0.10	SEQ ID NO: 30
CTCCCGCCATAAAAAAACTCATGTTTC	63.37	-0.10	SEQ ID NO: 31
TCCCGCCATAAAAAAACTCATGTTCAA	62.86	-0.10	SEQ ID NO: 32
CCCGCCATAAAAAAACTCATGTTCAA	60.47	-0.10	SEQ ID NO: 33
CCCCATAAAAAAACTCATGTTCAAG	57.98	-0.10	SEQ ID NO: 34
CCCCATAAAAAAACTCATGTTCAAGA	56.20	-0.10	SEQ ID NO: 35

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cont

Clusters of retained oligonucleotides are identified and ranked based on cluster size. In this example a contiguous cluster of 13 retained oligonucleotides is identified by the vertical black bar on the left. All of the oligonucleotides in this cluster may be evaluated experimentally.

GTCCAAAAAGGGTCAGTCTACCTCCGCCATAAAAAACTCATGTTCAAGA (target complement sequence) (SEQ ID NO: 9)

	T <sub>m</sub> (°C)	ΔG <sub>MFOLD</sub>	
GTC	71.77	-1.20	SEQ ID NO: 10
TC	71.99	-1.20	SEQ ID NO: 11
CC	70.78	-1.20	SEQ ID NO: 12
CA	71.23	-1.20	SEQ ID NO: 13
AA	73.07	-1.20	SEQ ID NO: 14
AAA	75.68	-1.20	SEQ ID NO: 15
AAAC	77.53	-1.20	SEQ ID NO: 16
AAACG	79.03	-1.20	SEQ ID NO: 17
AAACGT	79.03	-1.20	SEQ ID NO: 18
AAACGTC	76.85	-1.20	SEQ ID NO: 19
AAACGTC	73.10	-0.00	SEQ ID NO: 20
GTC	69.50	0.90	SEQ ID NO: 21
TCAG	65.60	0.90	SEQ ID NO: 22
CAGT	64.96	0.90	SEQ ID NO: 23
AGT	65.48	1.10	SEQ ID NO: 24
GTC	66.36	2.40	SEQ ID NO: 25
TCT	64.97	2.90	SEQ ID NO: 26
CTAC	63.96	2.70	SEQ ID NO: 27
TAC	62.58	1.10	SEQ ID NO: 28
ACCT	65.10	0.40	SEQ ID NO: 29
CCT	64.96	0.10	SEQ ID NO: 30
CTCC	63.37	-0.10	SEQ ID NO: 31
TCCC	62.86	-0.10	SEQ ID NO: 32
CCCG	60.47	-0.10	SEQ ID NO: 33
CGGC	57.98	-0.10	SEQ ID NO: 34
GGCC	56.20	-0.10	SEQ ID NO: 35

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cont